

What is claimed is:

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5 1. An improved process for reacting a terminal alkyne with an azide for forming a triazole, wherein the improvement comprises:

catalyzing said reaction by addition of a catalytic amount of a metal salt having a metal ion selected from the group consisting of Cu, Au, Ag, Hg, Cd, Zr, Ru, Fe, Co, Pt, Pd, Ni, Pt, Rh, and W,

10 wherein the terminal alkyne may be either free in solution or attached to a supporting molecule, such as PEG .

2. An improved process for reacting a terminal alkyne with an azide for forming a triazole, wherein the improvement comprises:

5 catalyzing said reaction by addition of a catalytic amount of copper (I), wherein the terminal alkyne may be either free in solution or attached to a supporting molecule, such as PEG .

3. A process for reacting a terminal alkyne with an azide for forming a triazole comprising the following step:

10 catalyzing said reaction by addition of a metal salt having a metal ion selected from the group consisting of Cu, Au, Ag, Hg, Cd, Zr, Ru, Fe, Co, Pt, Pd, Ni, Pt, Rh, and W in the presence of a reducing agent for reducing said metal ion to a catalytically active form.

25 4. A process for reacting a terminal alkyne with an azide for forming a triazole comprising the following step:

catalyzing said reaction by the addition of Cu(II) in the presence of a reducing agent for reducing said Cu(II) to Cu(I) in catalytic amount.

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5. A process for reacting a terminal alkyne with an azide for forming a triazole comprising the following step:

performing said reaction in a solution in contact with a metal selected from the group consisting of Cu, Au, Ag, Hg, Cd, Zr, Ru, Fe, Co, Pt, Pd, Ni, Pt, Rh, and W, said metal contributing directly or indirectly to a catalysis of said reaction.

6. A process for reacting a terminal alkyne with an azide for forming a triazole comprising the following step:

performing said reaction in a solution contained, at least in part, in a metal vessel, the metal of the metal vessel being selected from the group consisting of Cu, Au, Ag, Hg, Cd, Zr, Ru, Fe, Co, Pt, Pd, Ni, Pt, Rh, and W, said metal contributing directly or indirectly to a catalysis of said reaction.

7. A process for reacting a terminal alkyne with an azide for forming a triazole comprising the following step:

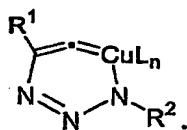
performing said reaction inside a cell, said cell containing a catalytic quantity of copper(I) sufficient to catalyze said reaction, said copper(I) contributing directly or indirectly to a catalysis of said reaction.

8. A process for reacting a terminal alkyne with an azide for forming a triazole comprising the following step:

performing said reaction in a solvent containing a catalytic amount of a metal ion selected from ions from the group of metals consisting of Cu, Au, Ag, Hg, Cd, Zr, Ru, Fe, Co, Pt, Pd, Ni, Pt, Rh, and W, said metal ion contributing directly or indirectly to a catalysis of said reaction, said metal ion being coordinated to a ligand for solubilizing said metal ion within said solvent, for inhibiting oxidation of said metal ion, and for dissociating, in whole or in part, from said metal ion during the catalysis of said reaction by said metal ion.

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9. A process according to Claim 8 wherein said ligand is acetonitrile.
10. A process according to Claim 8 wherein said ligand is a cyanide, nitrile, or isonitrile.
11. A process according to Claim 8 wherein said ligand is water.
12. A process according to Claim 8 wherein said ligand is selected from the group consisting of nitrile, isonitrile, primary or secondary amine, carboxylate, halide, alcohol, and thiol.
13. A process according to Claim 8 wherein said ligand is polyvalent and includes one or more functional groups selected from the group consisting of nitrile, isonitrile, primary or secondary amine, carboxylate, halide, alcohol, and thiol.
14. A reactive intermediate for producing a triazole, the reactive intermediate being represented by the following 6-membered ring structure:



wherein:

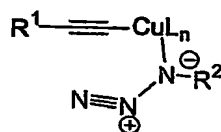
R<sup>1</sup> is a 4-triazole substituent,

R<sup>2</sup> is a 1-triazole substituent,

L is a Cu ligand, and

"n" is 1, 2, or 3.

15. A reactive intermediate for producing a triazole, the reactive intermediate being represented by the following structure:



wherein:

$\text{R}^1$  is a 4-triazole substituent,

$\text{R}^2$  is a 1-triazole substituent,

L is a Cu ligand, and

"n" is 1, 2, 3, or 4.

16. A two step process of derivatizing an amine containing molecule with a triazole, the process comprising the following steps:

Step A: derivatizing the amine containing molecule to form a terminal alkyne, then

Step B: ligating the product of said Step A with an azide containing molecule by addition of the azide containing molecule in the presence of a catalytic amount of Cu to form a triazole derivative of the amine containing molecule.

17. A one step process for producing a polyvalent triazole, the process comprising the following step:

derivatizing a polyazide core by addition of a molecule having a terminal alkyne in the presence of a catalytic amount of Cu.

18. A one step process for producing a polyvalent triazole, the process comprising the following step:

derivatizing a polyalkyne core by addition of an azide containing molecule in the presence of a catalytic amount of Cu.

## ABSTRACT OF THE DISCLOSURE

- 5           A metal catalyzed ligation process is employed to bind azides and terminal acetylenes to give triazoles. In many instances, the reaction sequence regiospecifically ligates azides and terminal acetylenes to give only 1,4-disubstituted [1,2,3]-triazoles.

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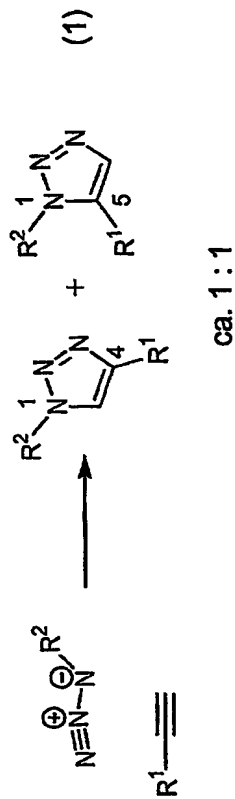


Figure 1A

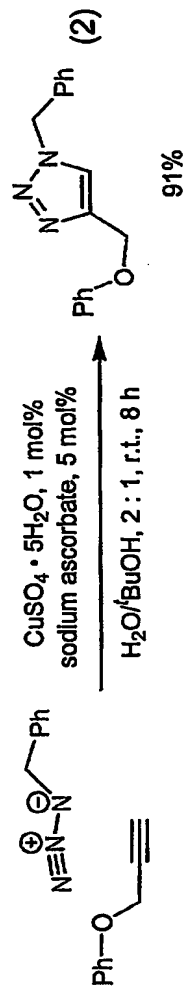


Figure 1B

Figure 2

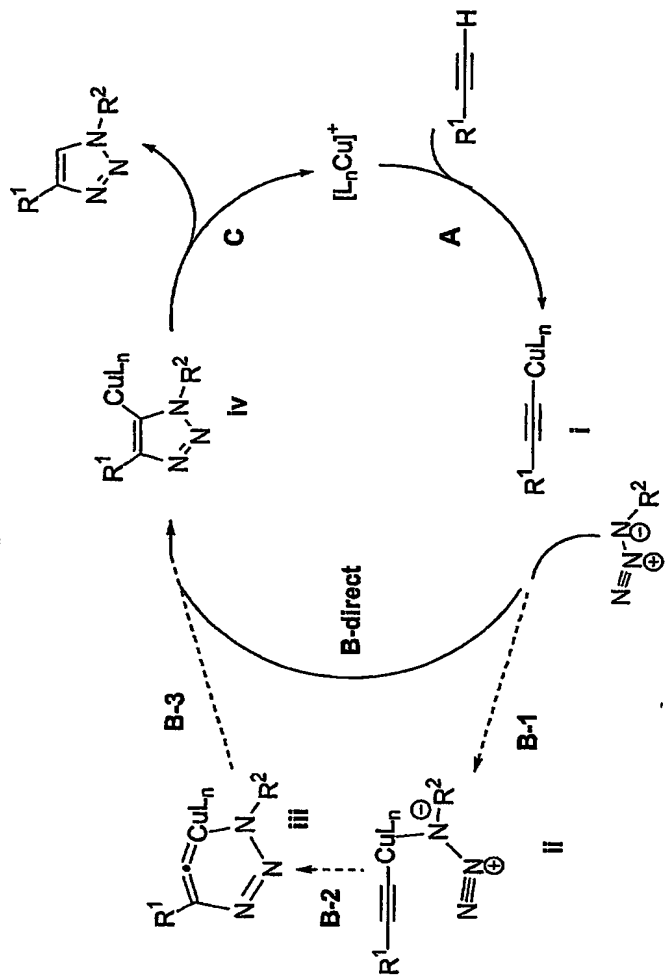
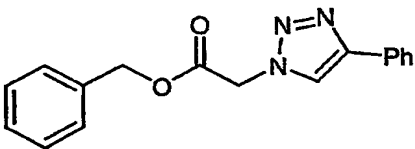
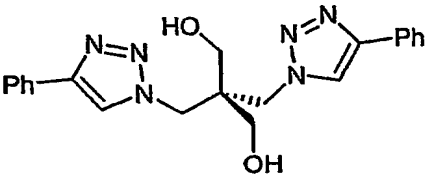
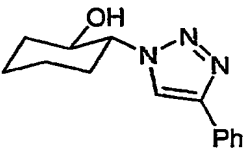
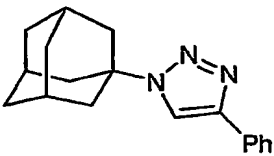
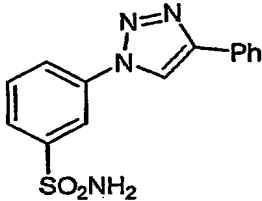


Figure 3A

Entry	Product	yield, %
1		94
2		93
3		82
4		84
5		92



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Figure 3B

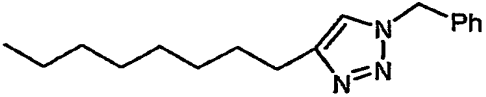
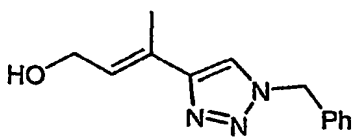
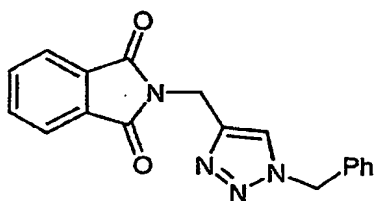
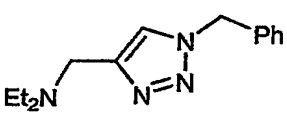
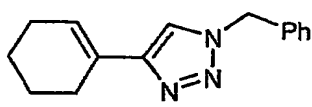
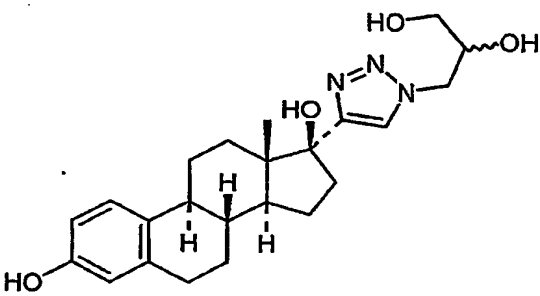
Entry	Product	yield, %
6		92
7		84
8		88
9		90
10		80
11		94

Figure 4

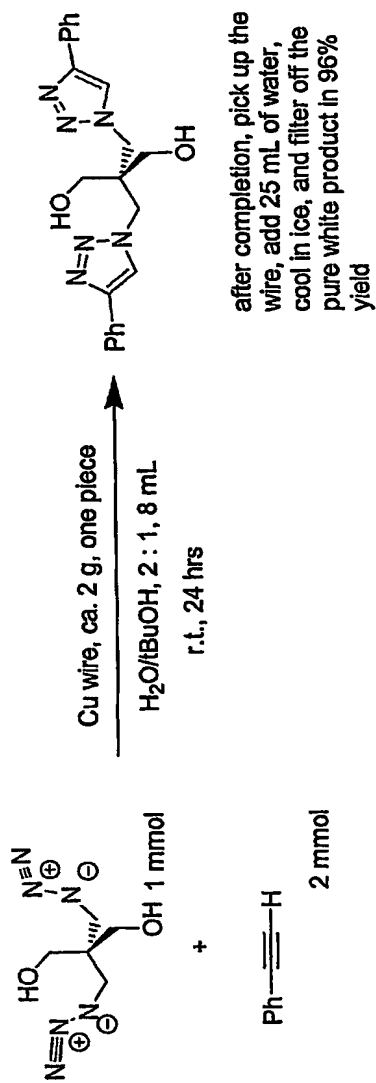
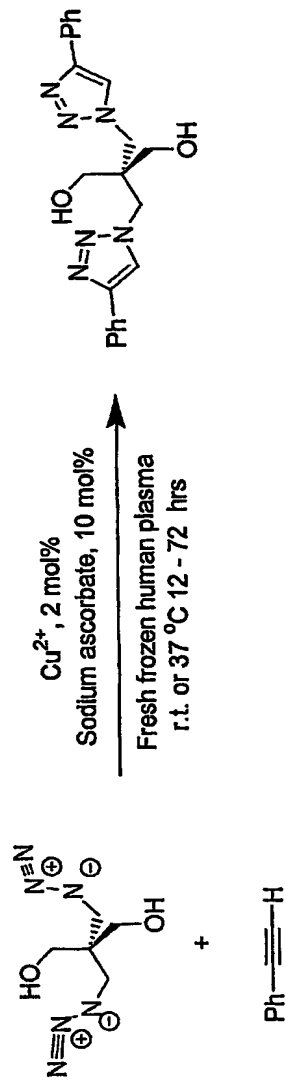
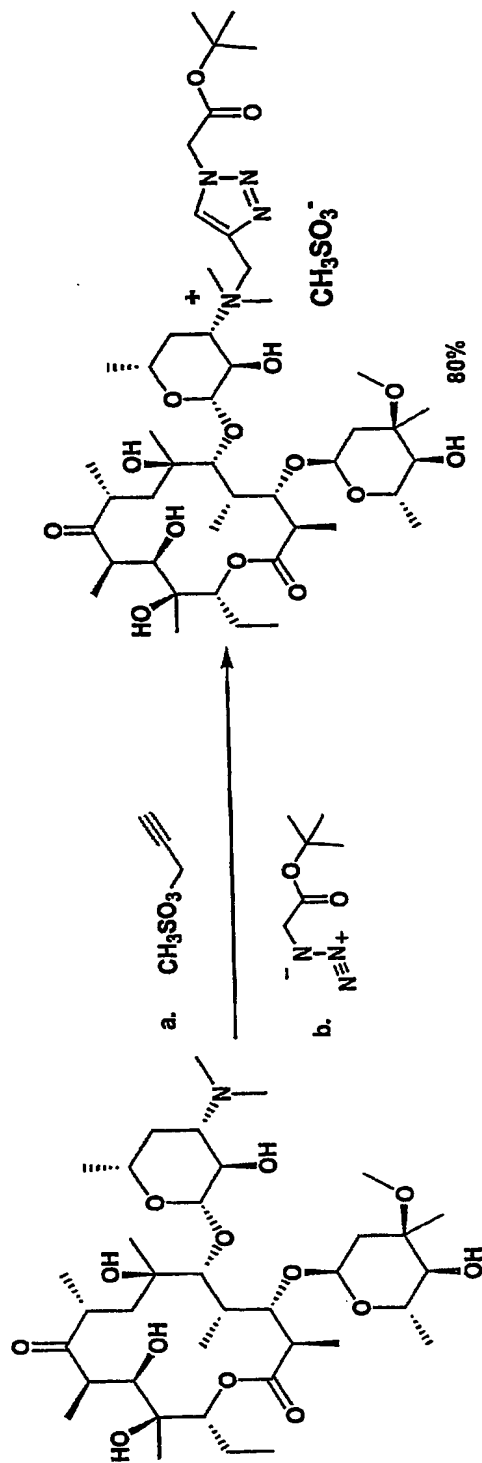


Figure 5



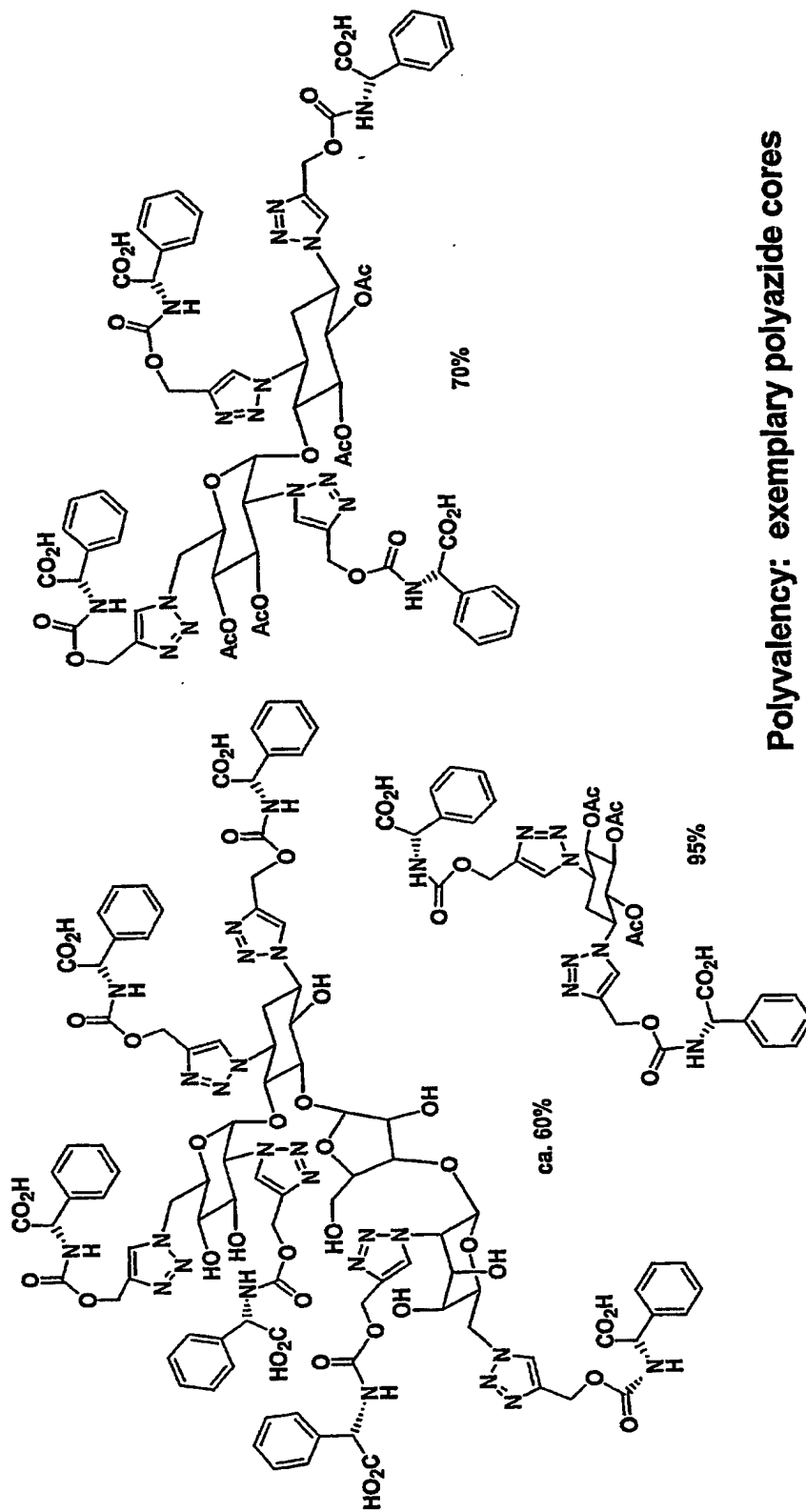
Human plasma as a solvent

Figure 6



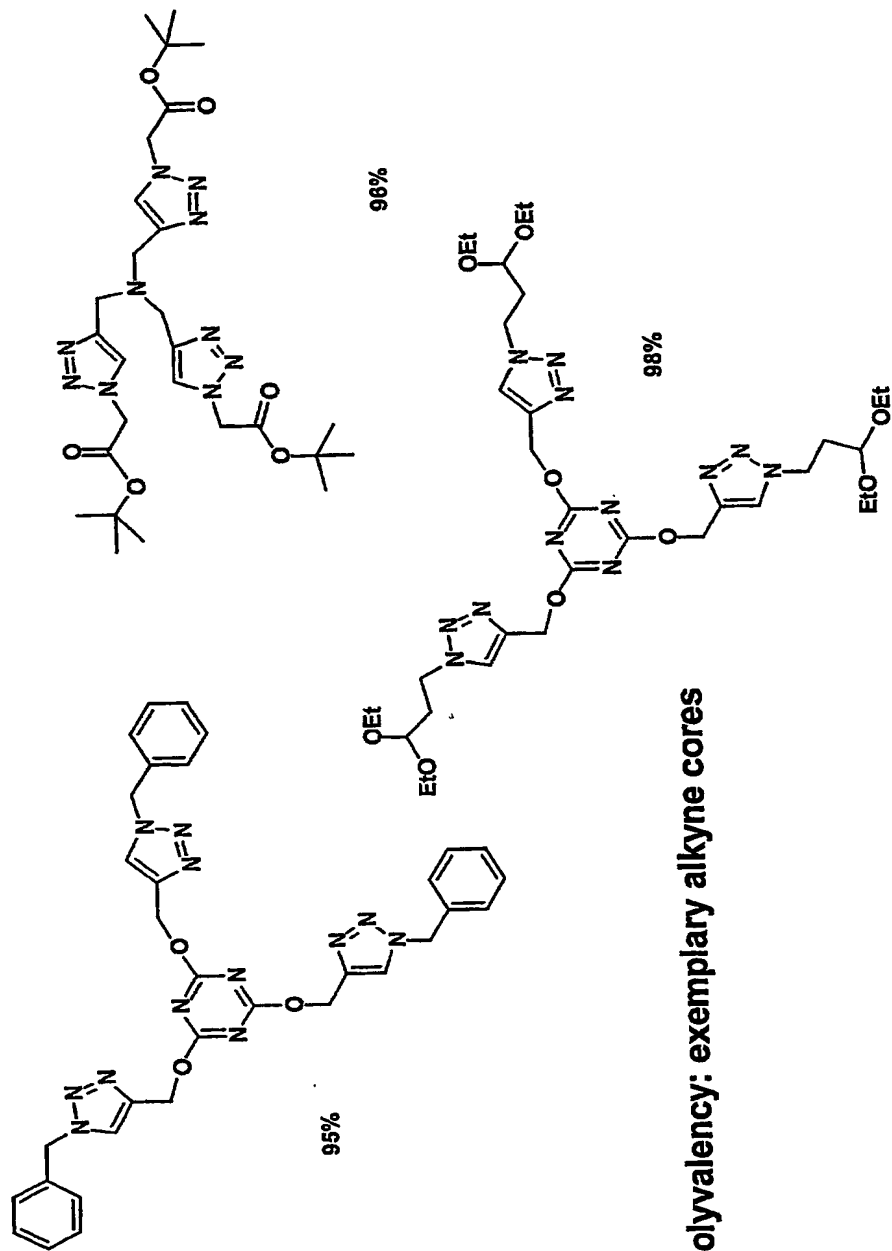
Facile derivatization of complex molecules:  
Erythromycin

Figure 7



Polyvalency: exemplary polyazide cores

Figure 8



Polyvalency: exemplary alkyne cores